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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JAGOE, DONNA A	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
05/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/619,426	TRACEY ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,13-18 and 21-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,13-18 and 21-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 11, 13-18 and 21-33 are pending in this application.

Applicants' arguments filed January 26, 2009 have been fully considered and they are deemed to be persuasive regarding previous rejections of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

However, upon reconsideration, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

The indicated allowability of claims 11, 13-18 and 21-25 is withdrawn in view of the newly discovered reference(s) to Bianchi et al. (JEM published 3/1/1996), Bukrinsky et al. U.S. Patent No. 5,574,040 and Otto U.S. Patent No. 5,616,578 A in view of the legal decision of In re Kerkhoven. Rejections based on the newly cited reference(s) follow.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites the limitation "wherein the disease or disorder is modulated" in lines 1-2 of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no recitation of “a disease or disorder” in instant claim 11 from which claim 13 depends.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11, 13-18 and 21-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bianchi et al., JEM March 1996 (U), Bukrinsky et al. U.S. Patent No. 5,574,040 and Otto U.S. Patent No. 5,616,578 A in view of the legal decision of In re Kerkhoven.

Bianchi et al. teach CNI-1493 is a tetravalent guanylhydrazone that inhibits cytokine-inducible arginine transport and nitric oxide production in macrophages (see abstract). Further it suppressed the lipopolysaccharide (LPS)-stimulated production of proinflammatory cytokines (tumor necrosis factor (TNF), interleukins 1β and 6, macrophage inflammatory proteins 1α and 1β) from human peripheral blood mononuclear cells (abstract). Further, Bianchi teaches that a relative overproduction of TNF occurs in patients with *inter alia*, HIV infection. Studies show that a tetravalent guanylhydrazone selectively and reversibly inhibits pro-inflammatory cytokine synthesis in vitro, and attenuates in vivo TNF production and endotoxemic death. Bianchi et al. teach that guanylhydrazone compounds may be useful in the treatment of diseases mediated by an overproduction of pro-inflammatory cytokines (page 935, columns 1-2). While the reference does not specifically state that CNI-1493 treats HIV, it states that CNI-1493 attenuates in vivo TNF production and it states that patients with HIV

overproduce TNF. It would have been obvious to one having ordinary skill in the art at the time the invention was made to employ a tetravalent guanylhydrazone such as CNI-1493 to treat HIV motivated by the teaching of Bianchi et al. who discloses that patients with HIV overproduce TNF and that guanylhydrazones such as CNI-1493 attenuates TNF production. Regarding the disease or disorder modulated by inhibiting the signaling along a pathway within the cascade, Bianchi et al. teach that CNI-1493 inhibits macrophage activation at an early stage in the intracellular signaling pathway (page 930, column 2, 1st paragraph). This is reasonably interpreted as inhibition of signaling along the pathway within the cascade. The compound CNI-1493 reads on the compounds of claims 21-25 in that Z is A-$(CH_2)_n$-A-, n is 2-10, A is NH(CO) and X_1, X_2, X'_1 and X'_2 is $GhyCCH_3$ (claim 21); Z is A-$(CH_2)_n$-A-, n is 3-8, A is NH(CO) and X_1, X_2, X'_1 and X'_2 is $GhyCCH_3$ (claim 22); Z is O-$(CH_2)_2$-O-, n is 2-10, X_1, X_2, is H, X'_1 and X'_2 is $GhyCCH_3$ (claim 23); Z is O-$(CH_2)_n$-O-, n is 2-10, X_2 is $GhyCCH_3$, and X_1, X'_1 and X'_2 is $GhyCCH_3$ (claim 24); and n is 3-8, X_2 and X'_2 is GhyCCH3 and X_1 and X'_1 is GhyCCH3 (claim 25). Bianchi et al. does not teach the administration of an additional therapeutic agent, such as a reverse transcriptase inhibitor, HIV protease inhibitor or a preintegration complex inhibitor. Regarding the salt, Bianchi et al. teach the tetrahydrochloride salt which is inclusive of the hydrochloride salt of instant claims 29 and 33 (page 927, column 2).

Bukrinsky et al. teach compounds and compositions for inhibition of HIV-1 preintegration complexes (nuclear importation) (see column 13, lines 15-32).

Otto teaches a method of treating HIV comprising administration of a reverse transcriptase inhibitor and a protease inhibitor (see abstract) such as AZT, ddI, ddC and d4T (see claim 1).

As stated in In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980):

> It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. In re Susi, 58 CCPA 1074, 1079-80, 440 F.2d 442, 445, 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21, 279 F.2d 274, 276-77, 126 USPQ 186, 188 (CCPA 1960). As this court explained in Crockett, the idea of combining them flows logically from their having been individually taught in the prior art.

Thus the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Accordingly, for the above reasons, the claims are deemed properly rejected and none are allowed.

Terminal Disclaimer

The terminal disclaimer filed on February 6, 2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 6,673,777 and 6,143,728 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe /D. J./
Examiner
Art Unit 1614

April 29, 2009

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614